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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,139	08/08/2001	Rosanne M. Crooke	ISPH-0596	3066

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EXAMINER	
SCHULTZ, JAMES	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,139	CROOKE ET AL.	
	Examiner	Art Unit	
	J. D. Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2004 and 17 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-10,12,13,15 and 21-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10, 12, 13, 15, and 21-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☒ Other: Seq. Alignment.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed June 16 and June 17 have been considered. Rejections and/or objections not reiterated from the previous office action mailed March 16, 2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Applicant's arguments and affidavit filed under 37 CRF § 1.132 with respect to claims rejected under 35 U.S.C. § 103(a) have been considered but are moot in view of applicant's amendment, which obviates the rejection under 35 U.S.C. § 103(a). A new grounds of rejection follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-10, 12, 13, 15, and 21-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Applicants amended claims 4-10, 12, 13, 15, and 21-29 are drawn to compounds 8 to 50 nucleotides in length targeted to nucleobases 1634 to 1769 of a nucleotide encoding human cholesterol ester transfer protein of SEQ ID NO: 3.

A thorough review of the specification and particularly of Table 1, which lists the oligos targeting SEQ ID NO: 3, indicates that applicants had not, previous to this amendment, disclosed targeting the entirety of the newly recited target region of 1634 to 1769 of a nucleotide encoding human cholesterol ester transfer protein of SEQ ID NO: 3. Accordingly, the instant specification is not considered to support claims directed to the region of 1634 to 1769, and is thus considered to introduce new matter. For example, applicants teach targeting using 20mer oligos nucleotides 1631 to 1658 and to 1671 through 1691 of the instant SEQ ID NO: 3, but do not teach targeting nucleotides 1659-1670 as now claimed. If applicant disagrees, applicant is invited to indicate with particularity by page and line number where such support exists for the targeting of the entirety of the region now claimed.

Claim Rejections - 35 USC § 103

Claims 4-10, 12, 13, 15, and 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olek *et al.* (WO 01/77384), in view of Ackerman *et al.* (U. S. Patent Number 6,001,992).

The claims of the above invention are drawn to antisense compounds 8 to 50 nucleotides in length that specifically hybridizes with nucleobases 1631 through 1769 of the instant SEQ ID

NO: 3, and inhibits the expression of human cholesterol ester transfer protein of SEQ ID NO: 3, and to such compounds that are contain phosphorothioate, 2'-O-methoxyethyl, or 5-methylcytosine modifications, and pharmaceutical preparations thereof.

The primer of Olek *et al.* (SEQ ID NO: 312150) possesses 100% complementarity with residues 1747-1758 of the instant application, and thus meets all the sequence limitations of the claims, and would accordingly specifically hybridize with human cholesterol ester transfer protein of SEQ ID NO: 3 (see attached sequence alignment). Furthermore, Olek *et al.* teaches that this primer is PNA modified, which is a common modification used in the art to enhance binding properties, and reduce nuclease degradation. Olek also teaches such compounds in solutions that are considered to be pharmaceutically acceptable. Olek does not teach said primer containing phosphorothioate, 2'-O-methoxyethyl, or 5-methylcytosine modifications.

Ackerman *et al.* teaches oligonucleotides containing phosphorothioate, 2'-O-methoxyethyl, or 5-methylcytosine modifications. Ackerman teaches that "[s]uch modified or substituted oligonucleotides are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases."

It would have been obvious to modify the oligo of Olek to contain the claimed modifications of phosphorothioate, 2'-O-methoxyethyl, or 5-methylcytosine because Olek teaches the oligo in PNA form, which is a common modification used in the art to enhance binding properties, and reduce nuclease degradation, and because Ackerman teaches that modified or substituted oligonucleotides are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic

acid target and increased stability in the presence of nucleases. Furthermore, such modifications are taught in detail by Ackerman, the steps of which are routine to one of ordinary skill.

Thus, in the absence of evidence to the contrary, the invention of the above claims would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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